REMARKS/ARGUMENTS

Reconsideration of this application and entry of the foregoing amendments are respectfully requested.

Claim 2 has been revised to include the limitations of now-cancelled claims 3 and 5. Claim 6 has been revised to define the invention with additional clarity. Support for the revision of claim 6 is found in the first full paragraph on page 6, where support for new claims 12 and 13 is also found. In addition to claims 3 and 5, claims 1 and 7 have also been cancelled without prejudice. That claims have been revised/cancelled should not be taken as an indication that Applicant agrees with any position taken by the Examiner. Rather, the revisions have been made merely to advance prosecution and Applicant reserves the right to pursue any deleted subject matter in a continuation application.

Claims 1-3 and 5-7 stand rejected under 35 USC 112, first paragraph, as allegedly being non-enabled. Withdrawal of the rejection is submitted to be in order for the reasons that follow.

The claims as now presented are drawn to a method of inhibiting melanin synthesis in the skin of a patient comprising administering directly to the patient's skin an amount of ZAG sufficient to effect the inhibition.

In rejecting the claims as non-enabled the Examiner contends that one cannot extrapolate from the teachings of the specification to the claimed method. In support of this assertion, the Examiner states:

> It is well know in the art that *in vitro* cultured cells have different characteristics than cells in the *in vivo* host animal.

The Examiner cites selected portions of Freshney, Dermer and Gura as basis for the statement. Applicant offers the following in connection with these documents.

Freshney admittedly points out general differences between behavior of cultured cells and the counterparts *in vivo*. However, Freshney also states that "Although the existence of such differences cannot be denied, it must be emphasized that many specialized functions are expressed in culture and as long as the limits of the model are appreciated, it can become a very valuable tool" (page 4, right column, second full paragraph).

In citing Dermer (a reference from 1994), the Examiner appears to be contending that because Dermer states that, in his opinion, "cell lines in which cancer is usually studied are unsuitable for the job", there are no meaningful cell culture models. Such an assertion is clearly without merit.

As regards Gura, this reference points up past problems in cancer drug discovery and includes a discussion of approaches being taken to develop better cancer models and the importance of defining molecular targets. It is not clear from the Examiner's comments why Gura is relevant to the present invention which is unrelated to cancer drug screening.

In rejecting the claims as non-enabled, the Examiner also contends that undue experimentation would be required to determine the amount of ZAG sufficient to inhibit melanin synthesis by topical administration of ZAG. The Examiner cites Poorsmans and Lei et al. The relevance of these references to the Examiner's point is not seen. It would be a matter of routine for one skilled in the art to determine an appropriate amount of ZAG to be administered to the skin of a patient. The amount selected would be that which provided the effect sought. No invention would be required to make that selection.

The Examiner's attention is directed to the fact that the Example provided in the application is based, at least in part, on the use of a widely used model of melanocyte function, B16 melanoma cells (see page 7, lines 1-3). The Examiner has offered nothing by way of evidence to indicate why this is not an appropriate model system. Indeed, submitted herewith are publications demonstrating the well-established nature of this model (see Jiménez-Cervantes et al, J. Cell Sci. 114:2335 (2001) (page 2339, last paragraph of Introduction) and validation of that model (Martinez-Esparza et al, Int. J. Biochem. Cell Biol. 33:971 (2001)) . In addition, the Examiner's attention is directed to the fact that the Example also includes a description of the inhibition by ZAG of melanin synthesis by normal melanocytes (see page 19). As pointed out, these studies indicate that ZAG has similar effects on melanin production in both normal and malignant melanocytes.

The revision of claim 6 is believed to address the Examiner's concerns as regards the term "aberrant".

In view of the above, reconsideration is requested.

This application is submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

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